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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/500,795	12/03/2004	Wenbin Dang	GPT-030.01	8669

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EXAMINER	
DICKINSON, PAUL W	
ART UNIT	PAPER NUMBER
1618	

NOTIFICATION DATE	DELIVERY MODE
08/10/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/500,795	DANG ET AL.	
	Examiner	Art Unit	
	PAUL DICKINSON	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 June 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9,12-18,20-22 and 25-30* is/are pending in the application.

4a) Of the above claim(s) *6,8 and 9* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5, 7, 12-18, 20-22 and 25-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's arguments, filed 6/17/2010, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objects are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Response to Arguments

Claim Rejections - 35 USC § 112, New Matter

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 1-5, 7, 12-18, 20-22, and 25-30 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, is maintained for the reasons of record.

Applicant argues that "wherein said composition provides extended release of said antineoplastic agent into said anatomic area; for a period of at least seven days, the rate of release of said antineoplastic agent is approximately constant" is supported on page 6, lines 16-24 of the application.

Applicant's arguments have been fully considered but are not found persuasive. Page 6, lines 16-24 recites:

> In certain embodiments, administration of the subject polymers results in sustained release of an encapsulated antineoplastic agent for an extended period of time and in an amount that is not possible with other modes of administration. In certain embodiments, release of the antineoplastic agent follows zero order kinetics, i.e. the rate of release is independent of the concentration of antineoplastic agent present. In some instances there will be an initial burst, or higher rate of release, followed by a steady zero-order release. In certain embodiments, the properties of the polymer:therapeutic complex are such that the burst is minimized.

Nowhere in this section does it show that Applicant contemplated "wherein said composition provides extended release of said antineoplastic agent into said anatomic area; for a period of at least seven days, the rate of release of said antineoplastic agent is approximately constant".

The Examiner maintains that the application does not support: "wherein said composition provides extended release of said antineoplastic agent into said anatomic area; for a period of at least seven days, the rate of release of said antineoplastic agent is approximately constant" The specification states that one embodiment of the invention, PACLIMER, provides a constant rate of release of paclitaxel (see Example 13). The specification does not contemplate an approximately constant rate of release over a representative number of embodiments of claim 1, which is directed to any antineoplastic agent released from any biocompatible polymer having the structure disclosed in claim 1. The specification further does not contemplate an "extended release of said antineoplastic agent into said anatomic area; for a period of at least seven days, the rate of release of said antineoplastic agent is approximately constant" over the scope of the invention. It was never contemplated that the invention would

provide these properties, except for Example 13. Therefore, the specification does provide written description for these properties over the scope of claim 1.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The rejection of claims 1-5, 7, 12-18, 20-22, and 25-30 under 35 U.S.C. 103(a) as being unpatentable over US 5651986 ('986) in view of US 6166173 ('173) is maintained.

Applicant argues the following two points:

(1) Applicant argues that the Examiner has used impermissible hindsight in rejecting the claims.

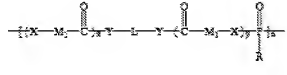
(2) Applicant argues that their invention provides unexpectedly improved benefits. On page 94, lines 18-23 of the specification, the method of using the PCPP-SA implant of '986 is discussed. The '986 method utilizes implants which release their antineoplastic agents in a biphasic pattern. The '986 method results in sporadic toxicity after implantation due to the initial burst of the drug. The skilled practitioner would have expected to see similar initial burst with the compositions employed in the claimed methods. However, page 94, lines 24-27 of the specification states that use of the claimed compositions unexpectedly

resulted in a constant *in vitro* rate of release, i.e. no initial burst. Data is given in Figure 1.

Applicant's arguments have been fully considered but are not found persuasive.

Regarding (1), '986 discloses a method of treating brain cancer (a central nervous system neoplasm) of a patient comprising: instilling into an anatomic area of a patient affected by brain cancer a therapeutically effective amount of a composition comprising a biocompatible polymer and an antineoplastic agent (see col 3, line 64 to col 4, line 15; col 11, line 62 to col 12, line 20). Paclitaxel is a preferred antineoplastic agent (see col 4, lines 10-15). The composition can be administered alone or in combination with, either before, simultaneously, or subsequent to, treatment using other chemotherapeutic or radiation therapy or surgery (see col 11, lines 62-67; col 12, lines 21-24; col 18, lines 14-16). '986 fails to teach the polymer of formula VIIf disclosed in instant claim 25.

'173 discloses a composition comprising a biocompatible polymer and an antineoplastic agent wherein the biodegradable polymer has the following formula:



Wherein

X may be -O-;

M_1 may be a branched aliphatic group having from 1-20 carbon atoms, such as methylene or 1-methylethylene;

Y may be -O-;

L may be a straight chain aliphatic group having from 1-20 carbon atoms, such as ethylene; and

R may be an alkoxy, such as –OEt.

(see abstract; col 6, line 40 to col 7, line 39). Except for M_1 (see below), this polymer corresponds to Formula VIIf as disclosed in instant claims 25-30. Paclitaxel is a preferred antineoplastic agent (see col 20, line 66 to col 21, line 5). The composition provides effective sustained drug release of the compound for a number of applications (see col 21, line 22 to col 22, line 33).

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to incorporate the biodegradable, sustained release polymer composition of '173 into the method taught by '986. In this way, a sustained release implant comprising an antineoplastic agent will be made that is effective to treat brain cancer.

The polymer of '173 differs from that of instant formula VIIf in that the polymer of '173 teaches branched aliphatic groups having from 1-20 carbon atoms, but does not explicitly teach an embodiment wherein M_1 = methylmethylene (-CH(CH_3)-), which corresponds to instant formula VIIf. It is the opinion of the Examiner that an embodiment of the polymer of '173 where M_1 = methylmethylene is obvious in view of the teaching of '173, and therefore instant formula VIIf is obvious in view of the teaching of '173. '173 teaches aliphatic

groups having from 1-20 carbon atoms. '173 favors the lower end of this range, as seventeen of the thirty-one total examples at col 7, lines 19-38 contain five carbons or less. '173 teaches M_1 = methylene (-CH_2-) and M_1 = 1-ethylmethylene (-CH(CH_3)-CH_2-). M_1 = methylene (-CH_2)- ('173) and methylmethylene (-CH(CH_3)-) (instant formula VIIf) differ in the presence of a -CH_3 group. To modify a methylene ('173) to produce a methylmethylene (instant formula VIIf), a -H would need to be replaced with a -CH_3. M_1 = 1-methylethylene (-CH(CH_3)-CH_2-) ('173) and methylmethylene (-CH(CH_3)-) (instant formula VIIf) differ in the presence of a -CH_2-. To modify 1-methylethylene ('173) to produce methylmethylene (instant formula VIIf), a -CH_2- would need to be removed. Substituting a methyl for a hydrogen or modifying the number of methylene groups in a chain are common modifications performed in the chemical arts. It is the position of the Examiner that 1-methylethylene ('173) and methylene ('173) are obvious variants over methylmethylene (instant formula VIIf) and for this reason, in combination with the fact that M_1 = methylmethylene is an embodiment of the overall M_1 taught by '173 (i.e. a branched aliphatic group having from 1-20 carbon atoms), that instant formula VIIf is rendered obvious by the teaching of '173.

The references do not explicitly teach that this composition would "provide extended release of said antineoplastic agent into said anatomic area; for a period of at least seven days, the rate of release of said antineoplastic agent is approximately constant". A composition cannot, however, be separated from its properties. Therefore, the instantly claimed release characteristics must be an

inherent property of the composition. The polymeric composition rendered obvious by '986 in view of '173 meets all the structural limitations of the currently claimed invention. Therefore the polymer composition of '986 in view of '173 must inherently provide extended release of the antineoplastic agent into said anatomic area; for a period of at least seven days, the rate of release of said antineoplastic agent is approximately constant. "'[T]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer.' Atlas Powder Co. v. Ireco Inc., 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977)." MPEP § 2112, I.

Nowhere in the above analysis did Examiner rely on Applicant's disclosure. The rejection is based solely on the prior art and knowledge generally available to the ordinary artisan.

Regarding (2), page 94 of the specification does not cite US 5651986, but refers to a "previous report" examining paclitaxel delivery via PCPP-SA implants in rodent models of malignant brain tumors. Applicant's reply states that the "previous report" at page 94, line 18 is US 5651986 ('986). As the specification does not make this connection, however, the Examiner has no way of knowing if the composition discussed on page 94 of the specification is the same

composition as '986. Without evidence supporting that the "previous report" is '986, the Examiner cannot take the attorneys word that the "previous report" is '986. As such, a proper analysis cannot be given.

> "A showing of unexpected results must be based on evidence, not argument or speculation. In re Mayne, 104 F.3d 1339, 1343-44, 41 USPQ2d 1451, 1455-56 (Fed. Cir. 1997)" MPEP § 2145.

> "Compare Ex parte Gray, 10 USPQ2d 1922 (Bd. Pat. App. & Inter. 1989) (Claims were directed to human nerve growth factor b-NGF free from other proteins of human origin, and the specification disclosed making the claimed factor through the use of recombinant DNA technology. The claims were rejected as prima facie obvious in view of two references disclosing b-NGF isolated from human placental tissue. The Board applied case law pertinent to product-by-process claims, reasoning that the prior art factor appeared to differ from the claimed factor only in the method of obtaining the factor. The Board held that the burden of persuasion was on appellant to show that the claimed product exhibited unexpected properties compared with that of the prior art." MPEP § 2144.04.

> "Office personnel should avoid giving evidence no weight, except in rare circumstances. Id. See also In re Alton, 76 F.3d 1168, 1174-75, 37 USPQ2d 1578, 1582-83 (Fed. Cir. 1996). However, to be entitled to substantial weight, the applicant should establish a nexus between the rebuttal evidence and the claimed invention, i.e., objective evidence of nonobviousness must be attributable to the claimed invention." MPEP § 2145.

The Examiner acknowledges that Figure 1 of the instant application shows *in vitro* release profiles of paclitaxel from PACLIMER. However, Applicant has not met the burden of showing that the rebuttal evidence is unexpected over '986, that there is a nexus between the rebuttal evidence and the claimed invention (which is to a method for treating a central nervous system neoplasm of

a patient), nor shown that the results are commensurate in scope with the claimed method. See MPEP § 716.02 - § 716.02(g).

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to PAUL DICKINSON whose telephone number is (571)270-3499. The examiner can normally be reached on Mon-Thurs 9:00am-6:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

Paul Dickinson
Examiner
AU 1618

August 2, 2010

August 2, 2010